Myocardial infarction and alcohol consumption: A population-based case-control study

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Abstract *Background and aim:* Coronary heart disease (CHD) is the leading cause of death in industrialized societies. Identifying and characterizing modifiable variables associated with CHD is an important issue for health policy. The aim of the present study was to analyze the association of non-fatal myocardial infarction with total alcohol consumption and type of alcoholic beverage consumed. Preference of the subjects' consumption for beer, wine, or spirits was set at 80% or more of total alcoholic beverage consumption.

Methods and results: A population-based case-control study (244 subjects and 1270 controls) was conducted. Male patients aged 25 to 74 years with first myocardial infarction (MI) were recruited in the same region as the healthy male controls, who were taken from a random sample representative of the Gerona population. Alcoholic beverage consumption during the preceding week was recorded. Multiple logistic regression analysis was performed to determine the association of alcohol consumption and non-fatal MI.

Total alcohol consumption up to 30 g per day, adjusted for lifestyle and cardiovascular risk factors, was inversely associated (Odds ratio 0.14; 95% confidence interval 0.06—0.36) with the risk of non-fatal MI. Drinking up to 20 g of alcohol through wine, beer and spirits significantly decreased the adjusted risk of MI. Higher alcohol intake did not substantially reduce the risk. A preference for spirits was correlated with a significantly increased risk of non-fatal MI ($P < 0.05$).

Conclusion: Moderate alcohol consumption, independent of the type of alcoholic beverage, was associated with non-fatal MI risk reduction.

Introduction

Alcohol is an important constituent of the diet of industrialized societies. Although total alcohol consumption per capita has slightly decreased during the past 20 years in Spain, it can still be considered high in comparison with other European countries [1].

Coronary heart disease (CHD) is the leading cause of death in industrialized and developing countries [2]. Every year in Europe, there are between 200 and 800 new cases of myocardial infarction (MI) per 100,000 men aged between 35 and 64 years [3,4]. Ischemic heart disease (IHD) produces more than 70,000 hospital admissions per year in Spain [4] and continues to be the primary cause of death in men and the third most important cause of death in women, being responsible for 11% and 10% of deaths in men and women, respectively, in 1997 in Spain [5].

Alcohol consumption exerts adverse effects on health [6,7]. In contrast, firm scientific evidence suggests a U- and L-shaped relationship between alcohol consumption and total and CHD mortality, respectively [8,9]. Alcohol drinking, in particular moderate alcohol consumption, has been favorably associated with non-fatal MI and CHD mortality [10–12]. Furthermore, it has been suggested that the polyphenolic content of alcoholic beverages, particularly of wine, exerts an additional protective effect against CHD [13–16]. Indeed, the widespread consumption of wine has been held responsible for part of the low incidence of CHD in France despite a high consumption of saturated fat [17,18]. However, there is no conclusive evidence as to whether the favorable effects of alcoholic beverages on CHD are mediated solely by the alcohol content or whether the polyphenolic compounds also play a role.

There is little information on the association between type of alcoholic beverages consumed and CHD risk in southern European countries. Beyond the necessity to decrease overall alcohol consumption in these countries, it is fundamental to elucidate whether the above-mentioned protective effects on CHD are also present.

The aim of the present study was to determine the association of quantity and type of alcohol consumption with the CHD risk in a southern European population.

Methods

Study subjects

A population-based case-control study was conducted in Gerona, Spain. Cases totaled 244 consecutive male patients enrolled between 1999 and 2000. Patients were examined during hospitalization; inclusion criteria were: (1) age 25–74 years and (2) presence of a first myocardial infarction. Patients were recruited in the same region as the healthy male controls ($n = 1270$), who were taken from a random sample representative of the Gerona population The response rate of controls was 71%. This study and the registry are both part of the REGICOR project (*REgistre GIroní del COR* or Gerona Heart Registry) [19,20].

Alcohol consumption

Participants were asked to report their alcohol consumption over the preceding week, using a structured open-ended questionnaire that ascertained the consumption of alcoholic beverages typical of the region (beer, wine and spirits). The assumption for average alcohol gradation (%) of beer, wine and spirits was 5.0%, 12.5% and 40.0%, respectively. Alcohol intake (g/day) was calculated by multiplying the amount of the beverage (mL), the respective gradation (%), and the constant 0.80 to transform alcohol volumes into weight (g). The cut-off to establish preference for an alcoholic beverage was set at 80% of the participant's total alcohol consumption. Participants were not asked about alcohol drinking cessation. Therefore, all former alcohol drinkers were included in the analysis as participants with 0 g of alcohol consumption.

Blood pressure

Two blood pressure (BP) determinations were taken by trained personnel using a periodically calibrated mercury sphygmomanometer with strict standard procedures.

Laboratory measurements

Blood samples were obtained after a 14-h fast. Serum was immediately frozen at −120 °C in liquid

nitrogen for transport and stored at −80 °C for final conservation. Total cholesterol and high-density lipoprotein (HDL) cholesterol were analyzed by standardized enzymatic methods (Roche Diagnostic, Basel, Switzerland) adapted to a Cobas Mira Plus autoanalyzer (Hoffmann-La Roche, Basel, Switzerland). Serum concentration was determined by an immunoturbidimetric method (Immunoturb Lp(a), Immuno Diagnostica, Vienna, Austria). Analyses were performed in a Cobas Mira Plus (Roche Diagnostic, Basel, Switzerland). Plasma fibrinogen concentration was determined using a coagulometric autoanalyzer (Toa Medical Electronics Co. Ltd, Kobe, Japan).

Smoking

Information on smoking habits of the participants was obtained by a structured standard interview. Participants were categorized as people who had never smoked, former smokers (<1 year), former smokers (>1 year) and current smokers (at least 1 cigarette/day on average during the last year). The latter were asked to state the average daily number of cigarettes smoked.

Leisure-time physical activity

Leisure-time physical activity was measured by the Minnesota Leisure-Time Physical Activity questionnaire. This questionnaire has been previously validated for Spanish men and women [21,22]. Participants were provided with detailed instructions and a list of physical activities, and asked to mark those activities that they had undertaken during the past year. The number of times this activity had been performed and the average duration of each occasion were then recorded. Each physical activity had an intensity code obtained in standardized experimental situations, based on the ratio between the metabolic rate during work and the basal metabolic rate [23]. An estimation of energy expenditure in the leisure-time physical activity in metabolic equivalent (MET) was obtained. One MET, the energy expended by sitting quietly, is equivalent to 3.5 mL of oxygen uptake per kilogram of body weight per minute [23]. A sedentary lifestyle was defined as an energy expenditure during leisure time lower than 1000 METs per minute per week.

Educational status

Maximum level of education attained was elicited, and for analysis purposes was recorded as illiterate, primary school, secondary school and university.

Statistical analysis

Differences in continuous variables were compared using the Student t-test. Categorical variables were tested using the χ^2 test. Age-adjusted logistic regression analysis was used to analyze the association of alcohol consumption (0 g/day, $>0\,g \leq 20\,g$, $>20\,g \leq 30\,g$, and $>30\,g$ per day; categorical) with MI. In addition to age, the following variables were introduced in further multiple logistic models to estimate the independent association of alcohol consumption and the risk of MI: leisure-time physical activity (one MET), educational status (illiterate, primary school, secondary school, and university; categorical), current smoking (binary; categorical), total cholesterol (mg/dL, continuous), LDL-cholesterol (mg/dL, continuous), HDL-cholesterol (per mg/dL), diabetes (binary), hypercholesterolemia drug treatment (binary) and diagnosed hypertension (binary). Missing values of total cholesterol, HDL-cholestrol, and LDL-choelstrol among subjects and controls were 76 and 186, respectively. For this reason, final mulivariate analysis was performed with 168 subjects and 1084 controls. The median of alcohol cosnumption among this number of subjects and controls was 11.1 g and 13.4 g, respectively. Differences were considered statistically significant at $P < 0.05$. Statistical analyses were performed by the SPSS software package version 12.0 for Windows (SPSS Inc., Chicago, IL).

Results

Subjects with MI were older than controls, more likely to be smokers and had higher prevalence of diabetes and hypertension than controls (Table 1). In addition, higher plasma levels of total, HDL-, and LDL-cholesterol were found in controls as compared to patients with MI (Table 1). In contrast, plasma triglyceride levels were higher in patients with MI than in controls (Table 1).

The age-adjusted risk of MI was significantly decreased with low levels of alcohol consumption (Table 2). Further controlling for lifestyle variables did not attenuate this association. The consumption of amounts above 30 g per day, although still significant, did not improve or inhibit the risk reduction. The association of alcohol consumption of more than 30 g per day and the risk of MI was attenuated after additional adjustment for several

Table 1 Characteristics of the study population consisting of consecutive male patients with first myocardial infarction and healthy controls representative of a population living in the same area

	MI Cases ($n = 244$)	Controls ($n = 1270$)	P
Age (years)	58.8 (10.9)	50.2 (13.5)	<0.01
Smoking (%)	41.0	27.0	<0.01
Diabetes (%)	22.0	13.0	<0.01
Diagnosed hypertension (%)	44.0	24.0	<0.01
Cholesterol total (mg/dL)	198.6 (36.6)	220.5 (42.0)	<0.01
HDL cholesterol (mg/dL)	39.9 (9.2)	47.4 (12.4)	<0.01
LDL cholesterol (mg/dL)	131.8 (31.0)	148.7 (37.4)	<0.01
Triglycerides (mg/dL)	135.4 (66.5)	124.5 (88.2)	<0.01
Body mass index (kg/m^2)	27.4 (3.9)	27.8 (4.0)	n.s.
Leisure-time physical activity (METs)	392.7 (418.3)	393.2 (3859)	n.s.
Educational level[a] (%)	29.4	33.0	n.s.
Total alcohol consumption (g/day)[b]	11.1 (32.8)	13.3 (18.0)	n.s.
Wine consumption (g alcohol/day)[b]	8.5 (233)	10.0 (12.3)	n.s.
Beer consumption (g alcohol/day)[b]	0.0 (8.6)	1.1 (9.2)	n.s.
Spirit consumption (g alcohol/day)[b]	0.0 (8.6)	0.0 (6.2)	n.s.
Wine preference[c]	43.9	42.1	n.s.
Beer preference[c]	70	10.4	n.s.
Spirit preference[c]	5.3	3.2	n.s.

MI, myocardial infarction; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MET, metabolic equivalent; n.s., not significant.
[a] More than secondary school.
[b] Median.
[c] More than 80% of total alcohol consumption consists of the corresponding beverage.

cardiovascular risk factors. In contrast, the risk reduction was not affected by this adjustment for alcohol consumption of less or equal than 30 g per day.

Table 3 shows the association of wine, beer, and spirit consumption with the risk of myocardial infarction. Multivariate logistical regression analysis revealed that consumption of wine, beer, and spirits (consumption of >0 g and ≤20 g alcohol/day) reduced the risk of MI by 78%, 76% and 79%, respectively, in comparison with non-alcohol drinkers. The consumption of alcohol from wine and beer above 30 g per day, although still significant, did not improve or inhibit the risk reduction.

The preference for a given alcoholic beverage and its relationship with the risk of MI is shown in Table 4. Subjects were classified as preferring beer, wine, or spirits when they reported a beverage category as constituting more than 80% of their alcohol intake. Preferences for spirits showed a significant increased risk of MI compared to mixed alcoholic beverage drinkers.

Discussion

The results of the present study suggest that moderate alcohol consumption significantly reduces the risk of non-fatal MI. Higher alcohol intake did

Table 2 Odds ratio (OR) and 95% confidence interval (CI) of myocardial infarction according to alcohol consumption

Alcohol (g/day)	Cases/control	Model 1[a]	Model 2[b]	Model 3[c]
		OR (95% CI)	OR (95% CI)	OR (95% CI)
0	40/45	1	1	1
>0 ≤ 20	125/806	0.19 (0.12–0.31)	0.24 (0.14–0.42)	0.22 (0.11–0.44)
>20 ≤ 30	22/189	0.14 (0.07–0.26)	0.13 (0.06–0.27)	0.14 (0.06–0.36)
>30	57/230	0.34 (0.20–0.58)	0.35 (0.19–0.66)	0.50 (0.23–1.15)

[a] Adjusted for age.
[b] Adjusted for variables of model 1 and additionally for smoking, educational level, and leisure-time physical activity.
[c] Adjusted for variables of model 2 and additionally for total cholesterol, LDL-cholesterol, HDL-cholesterol, diabetes, hypercholesterolemia drug treatment, and diagnosed hypertension.

Table 3   Odds ratio (OR) and 95% confidence interval (CI) of myocardial infarction according to consumption of alcoholic beverages

	Cases/control	Model 1[b] OR (95% CI)	Model 2[c] OR (95% CI)
Wine (g alcohol/day)[a]			
0	40/45	1	1
>0 ≤ 20	141/919	0.21 (0.12—0.35)	0.22 (0.11—0.47)
>20	36/136	0.30 (0.16—0.56)	0.32 (0.13—0.82)
Beer (g alcohol/day)[a]			
0	40/45	1	1
>0 ≤20	67/561	0.17 (0.09—0.31)	0.24 (0.10—0.52)
>20	12/87	0.22 (0.09—0.52)	0.22 (0.06—0.82)
Spirit (g alcohol/day)[a]			
0	40/45	1	1
>0 ≤ 20	65/435	0.23 (0.12—0.44)	0.21 (0.08—0.54)
>20	10/19	0.81 (0.30—2.20)	0.88 (0.18—4.37)

[a] Reference category: 0 g of total alcohol consumption.
[b] Adjusted for age and other alcoholic beverages.
[c] Adjusted for variables of model 1 and for smoking, educational level, leisure-time physical activity, total cholesterol, LDL-cholesterol, HDL-cholesterol, diabetes, hypercholesterolemia drug treatment, and diagnosed hypertension.

not further reduce the risk. Furthermore, the consumption of all types of alcoholic beverages (wine, beer, and spirits) was inversely associated with the risk non-fatal MI.

The average total alcohol consumption of the present population was comparable with that reported by the Spanish arm of the European Prospective Investigation into Cancer and Nutrition (EPIC) study [24]. In the present population, 23.4% of subjects and 18.1% of controls reported an average daily alcohol consumption of more than 30 g, which is approximately equivalent to more than 3 glasses (300 mL) of wine.

Epidemiological evidence has consistently linked alcohol consumption with lower risk of myocardial infarction [8]. Particularly, light to moderate (i.e. 10—30 g/day) alcohol consumption exerts a cardioprotective effect [25]. However, Mukamal and colleagues [10] showed in a large prospective study that even amounts of more than 50 g alcohol per day significantly reduced the risk of non-fatal myocardial infarction. The adverse effects of such amounts of alcohol might, however, overwhelm its cardioprotective effects. In the present study we observed a significant risk reduction of non-fatal MI for all alcohol drinking categories, although there was no improvement of risk reduction with amounts of more than 30 g of alcohol per day. It is worth mentioning that the odds ratio for MI with alcohol consumption of up to 30 g per day was not affected by controlling for several important lifestyle and cardiovascular risk factors. However, dietary intake data were recorded with different dietary assessment

Table 4   Odds ratio (OR) and 95% confidence interval (CI) of myocardial infarction according to alcoholic beverage preferences[a]

	Cases/control	OR (95% CI)[c]	OR (95% CI)[d]
Reference[b]	67/503	1	1
Wine preference	102/513	1.00 (0.70—1.42)	1.29 (0.76—2.20)
Beer preference	17/131	1.07 (0.60—1.91)	1.75 (0.82—3.71)
Spirit preference	13/41	2.21 (1.10—4.43)	2.89 (1.01—8.27)

[a] Preference: more than 80% of alcohol consumption coming from one beverage type (wine, beer, or spirits).
[b] Reference group: mixed alcohol consumer.
[c] Adjusted for age.
[d] Adjusted for age, total alcohol consumption, smoking, educational level, leisure-time physical activity, total cholesterol, LDL-cholesterol, HDL-cholesterol, diabetes, hypercholesterolemia drug treatment, and diagnosed hypertension.

methods in the two study surveys. Therefore, controlling the association of alcohol intake and cardiovascular risk factors for diet was not possible. This can be considered a limitation of the present study. On the other hand, it has been shown that controlling alcohol consumption for diet only slightly affects the risk of MI [10]. Wouters et al. have shown that the effect of alcohol consumption in the 24 h preceding myocardial infarction was strongly confounded by prodromal symptoms [26]. This fact can be considered to be a further limitation of the present study. We should also note, however, that we measured alcohol consumption in the 7 days before myocardial infarction. Therefore, the confounding effect of prodromal symptoms in this study might well be lower than that generally observed in the 24 h preceding myocardial infarction.

It has been suggested that non-alcoholic components of alcoholic beverages may exert a protective effect against CHD. This non-alcohol-specific effect, particularly observed for wine, is thought to be mediated through the antioxidant and vasorelaxant properties of its polyphenolic constituents [27,28]. However, the epidemiological evidence is inconclusive [29]. Recently, we found that the protective associations of wine consumption with several cardiovascular risk factors disappeared after controlling for level of alcohol consumption [30]. In the population of the present study, wine was the predominant alcoholic beverage, followed by beer and spirits. The risk of MI was significantly reduced for subjects exhibiting moderate wine, beer and spirit consumption.

This finding does not concur with the hypothesis that the predominant alcoholic beverage in a population is more likely to be inversely associated with MI. Mukamal and colleagues recently found that beer and spirits, the predominant alcohol beverages in their study population, significantly reduced the risk of MI. In contrast, wine, which was consumed less, showed no significant protective effect on MI [10]. Furthermore, it has been shown that the frequent consumption of an alcoholic beverage decreased the risk of MI [31].

Forty-three percent of the present population reported preferring wine to other alcoholic beverages, whereas 39.4% reported mixed alcoholic beverage consumption. The risk of myocardial infarction for wine and beer consumers was no different from mixed alcoholic beverage consumers. This association was not affected by lifestyle and cardiovascular risk variables. Additionally, adjusting for total alcohol consumption did not attenuate this relationship. In contrast,

preference for spirits strongly increased the risk of MI. Interestingly, Chou and colleagues found that a preference for spirits showed a direct association with elevated morbidity for several conditions [32]. However, in the present study, total alcohol consumption of subjects preferring spirits is less than 20 g per day. It has been noted that beverage preferences are accompanied by differences in lifestyle. Although we controlled for lifestyle factors including smoking, leisure-time physical activity and educational level, we were unable to control for several other variables. For example, wine drinking has been associated with healthier dietary habits [33]. Alcoholic beverage preferences have also been found to be related to differences in intellectual performance and personality characteristics [34,35]. It is unlikely that the observed risk associations of MI with spirit consumption were mediated by the alcohol component. It is more plausible that other lifestyle and/or socio-psychological factors account for the association of MI with spirit preferences.

In conclusion, total alcohol consumption of up to 30 g was inversely related to MI, independent of other lifestyle variables or cardiovascular risk factors. Furthermore, moderate wine, beer and spirit drinking significantly reduced the risk of MI in the present study population.

Acknowledgments

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